As stated in the Declaration, the inventor was not able to make the recombinant human neutral sphinogmyelinase (N-Smase) enzyme of claim 1 by using approaches that required peptide sequence information to make cloning probes. Declaration at ¶ 6-8.

However, the inventor stated he was able to make the recombinant human N-Smase by using a protein expression cloning method. Declaration at ¶ 9. Specifically, the inventor stated that the method used a monospecific antibody that he made. Declaration at ¶ 10. That monospecific antibody was not available to the pubic before December 1996. Declaration at ¶ 10.

The inventor also stated that the references cited in the outstanding §103 rejection (Chatterjee, Ogita and Ausbel) do not disclose or suggest how to make the monospecific antibody he made. Declaration at ¶13.

It is also stated that the references cited in the outstanding §103 rejection did not disclose or suggest that it would be impossible to make the recombinant N-Smase using standard protein sequencing techniques to make cloning probes. Declaration at ¶14.

All references mentioned in the Declaration are of record in this case.

Accordingly, and in view of reasons already of record, reconsideration and withdrawal of the outstanding obviousness rejection are respectfully requested. Early consideration and allowance of the application are earnestly solicited.

If for any reason a fee is required, a fee paid is inadequate or credit is owed for any excess fee paid, you are hereby authorized and requested to charge Deposit Account No. **04-1105**.

Respectfully submitted,

Date: 8 November 02

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Docket No. 46906-DIV2 (71699)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: S. Chatterjee

SERIAL NO.: 09/282,879 EXAMINER: M. Rao

FILED: March 31, 1999 GROUP: 1652

FOR: RECOMBINANT N-SMASEs AND NUCLEIC ACIDS ENCODING SAME

THE HONORABLE COMMISSIONER OF PATENTS AND TRADEMARKS
WASHINGTON, DC 20231

SIR:

DECLARATION PURSUANT TO 37 CFR 1.132

The undersigned declares as follows:

1. I am the inventor of the above-identified application (hereafter the "subject application"). Additionally, I am a Professor of Pediatrics in the Department of Pediatrics at the Johns Hopkins University Medical School in Baltimore, MD.

2. As I understand it, the subject application discloses and claims, among other things, a method of identifying a compound useful in the diagnosis or treatment of a human neutral sphingomyelinase (N-Smase) related disorder. A particular method includes contacting an agent with a recombinant N-Smase and analyzing enzyme activity in the presence and absence of the agent.

3. I have reviewed the Patent Office Action ("Office Action") dated April 9, 2002 issued in connection with the subject application. As I understand the Office Action, the patent Examiner rejected claims 13-17 as being obvious over Chatterjee et al. (*J. Biol. Chem.* (1989) 264: 12554); Ogita et al. (WO 95/18119); and Ausbel et al. (*Current Protocols in Molecular Biology*, J. Wiley & Sons (1987) pp. 10.0.3 –10.06).

Hereinafter, the cited references are referred to as "Chatterjee", "Ogita" and "Ausbel", respectively.

4. I am familiar with the contents of Chatterjee and Ausbel and I have read an English language translation of Ogita. As I understand it, Chatterjee reports isolation of naturally-occurring N-Smase from human urine, Ogita (as translated) reports isolation of a bacterial sphingomyelinase inhibitor from grass, and Ausbel discloses standard cloning methods.

5. I must respectfully disagree with the patent Examiner's position that the method I now claim is obvious over Chatterjee, Ogita and Ausbel. More specifically, I must disagree with the suggestion by the Examiner that it would be obvious to make the recombinant N-Smase featured in the claimed method.

6. For example, well before December 1996, I purified the N-Smase enzyme from human urine as described in Chatterjee. However, my attempt to obtain protein sequence information from the purified enzyme was not successful. Specifically, I found that the N-terminus of the N-Smase was blocked in a way that made it impossible to obtain useful protein sequence information using conventional methods.

7. Additionally, and well before December 1996, I contacted researchers at Harvard University (Cambridge, Mass) and asked them to obtain protein sequence information from the purified N-Smase enzyme at my direction. Using standard protein sequencing steps, they too were unable to obtain any useful protein sequence information from the purified enzyme.

8. I concluded that it was not possible to obtain useful protein sequence information from the purified N-Smase enzyme. I also concluded that it would not be

possible to make the recombinant N-Smase by using approaches that required peptide sequence information to make cloning probes.

9. I successfully made the recombinant N-Smase by using a protein expression cloning method.

10. In particular, and well before December 1996, I developed a monospecific antibody that bound the N-Smase enzyme. Preparation and use of that antibody was described in a research article I co-authored (Chatterjee, S. and N. Ghosh (1989) *J. Biol. Chem.* 21: 12554). The monospecific antibody I developed was not available to the public before December 1996.

11. I used the monospecific antibody to clone and isolate the recombinant human N-Smase featured in the claimed method. Particulars of the expression cloning approach I employed were provided in a research paper (Chatterjee, S et al. (1999) *J. Biol. Chem.* 24: 37407).

12. The expression cloning approach I used to clone and isolate the recombinant human N-Smase was not taught or suggested by Chatterjee, Ogita and Ausbel as cited by the Examiner.

13. In particular, there is no disclosure or suggestion in any of the cited references that it would be possible to make a monospecific antibody against human N-Smase and that the antibody could be used to clone and isolate the recombinant enzyme.

14. Additionally, there is no disclosure in any of the cited references that it would be impossible to clone and isolate the human N-Smase enzyme using standard protein sequencing techniques to make cloning probes.

15. I hereby further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: _____

_____
Subroto Chatterjee